

General

Guideline Title

Atrial fibrillation: the management of atrial fibrillation.

Bibliographic Source(s)

National Clinical Guideline Centre. Atrial fibrillation: the management of atrial fibrillation. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Jun. 49 p. (Clinical guideline; no. 180).

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Collaborating Centre for Chronic Conditions. Atrial fibrillation. National clinical guideline for management in primary and secondary care. London (UK): Royal College of Physicians; 2006. 173 p. [380 references].

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Recommendations are marked as [2006], [2006, amended 2014], [2010, amended 2012], [2012], [2013] or [new 2014]:

- [2006] indicates that the evidence has not been reviewed since 2006
- [2006, amended 2014] indicates that the evidence has not been reviewed since 2007, but changes have been made to the recommendation wording that change the meaning
- [2010, amended 2012] applies to guidance from NICE technology appraisal 197, published in 2010 and amended in 2012
- [2012] applies to guidance from NICE technology appraisal 249, published in 2012
- [2013] applies to guidance from NICE technology appraisal 275, published in 2013
- [new 2014] indicates that the evidence has been reviewed and the recommendation has been updated or added to.

The wording used in the recommendations in this guideline (for example, words such as 'offer' and 'consider') denotes the certainty with which the recommendation is made (the strength of the recommendation) and is defined at the end of the "Major Recommendations" field.

Diagnosis and Assessment

Perform manual pulse palpation to assess for the presence of an irregular pulse that may indicate underlying atrial fibrillation (AF) in people presenting with any of the following:

- Breathlessness/dyspnoea
- Palpitations
- Syncope/dizziness
- Chest discomfort
- Stroke/transient ischaemic attack [2006]

Perform an electrocardiogram (ECG) in all people, whether symptomatic or not, in whom AF is suspected because an irregular pulse has been detected. [2006]

In people with suspected paroxysmal AF undetected by standard ECG recording (paroxysmal atrial fibrillation spontaneously terminates within 7 days, usually within 48 hours):

- Use a 24-hour ambulatory ECG monitor in those with suspected asymptomatic episodes or symptomatic episodes less than 24 hours apart.
- Use an event recorder ECG in those with symptomatic episodes more than 24 hours apart. [2006]

Perform transthoracic echocardiography (TTE) in people with AF:

- For whom a baseline echocardiogram is important for long-term management
- For whom a rhythm-control strategy that includes cardioversion (electrical or pharmacological) is being considered
- In whom there is a high risk or a suspicion of underlying structural/functional heart disease (such as heart failure or heart murmur) that influences their subsequent management (for example, choice of antiarrhythmic drug)
- In whom refinement of clinical risk stratification for antithrombotic therapy is needed (see recommendations under "Assessment of Stroke and Bleeding Risks" and "Interventions to Prevent Stroke"). [2006, amended 2014]

Do not routinely perform TTE solely for the purpose of further stroke risk stratification in people with AF for whom the need to initiate anticoagulation therapy has already been agreed on appropriate clinical criteria (see Section 1.4 Assessment of stroke and bleeding risks and Section 1.5 Interventions to prevent stroke in the full version of the original guideline document). [2006, amended 2014]

Perform transoesophageal echocardiography (TOE) in people with AF:

- When TTE demonstrates an abnormality (such as valvular heart disease) that warrants further specific assessment
- In whom TTE is technically difficult and/or of questionable quality and where there is a need to exclude cardiac abnormalities
- For whom TOE-guided cardioversion is being considered. [2006]

Personalised Package of Care and Information

Offer people with AF a personalised package of care. Ensure that the package of care is documented and delivered, and that it covers:

- Stroke awareness and measures to prevent stroke
- Rate control
- Assessment of symptoms for rhythm control
- Who to contact for advice if needed
- Psychological support if needed
- Up-to-date and comprehensive education and information on:
 - Cause, effects and possible complications of AF
 - Management of rate and rhythm control
 - Anticoagulation
 - Practical advice on anticoagulation in line with recommendations in NICE clinical guideline 144
 - Support networks (for example, cardiovascular charities). [new 2014]

NICE has produced guidance on the components of good patient experience in adult NHS services. Follow the recommendations in [Patient experience in adult NHS services](#) (NICE clinical guideline 138). [new 2014]

Referral for Specialised Management

Refer people promptly at any stage if treatment fails to control the symptoms of AF and more specialised management is needed. [new 2014] (The

Guideline Development Group defined 'promptly' as no longer than 4 weeks after the final failed treatment or no longer than 4 weeks after recurrence of atrial fibrillation following cardioversion when further specialised management is needed.)

Assessment of Stroke and Bleeding Risks

Stroke Risk

Use the CHA₂DS₂-VASc stroke risk score to assess stroke risk in people with any of the following:

- Symptomatic or asymptomatic paroxysmal, persistent or permanent AF
- Atrial flutter
- A continuing risk of arrhythmia recurrence after cardioversion back to sinus rhythm. [new 2014]

Bleeding Risk

Use the HAS-BLED score to assess the risk of bleeding in people who are starting or have started anticoagulation. Offer modification and monitoring of the following risk factors:

- Uncontrolled hypertension
- Poor control of international normalised ratio (INR) ("labile INRs")
- Concurrent medication, for example concomitant use of aspirin or a non-steroidal anti-inflammatory drug (NSAID)
- Harmful alcohol consumption. [new 2014]

When discussing the benefits and risks of anticoagulation, explain to the person that:

- For most people the benefit of anticoagulation outweighs the bleeding risk
- For people with an increased risk of bleeding the benefit of anticoagulation may not always outweigh the bleeding risk, and careful monitoring of bleeding risk is important. [new 2014]

Do not withhold anticoagulation solely because the person is at risk of having a fall. [new 2014]

Interventions to Prevent Stroke

Do not offer stroke prevention therapy to people aged under 65 years with AF and no risk factors other than their sex (that is, very low risk of stroke equating to a CHA₂DS₂-VASc score of 0 for men or 1 for women). [new 2014]

Anticoagulation

Anticoagulation may be with apixaban, dabigatran etexilate, rivaroxaban or a vitamin K antagonist.

Consider anticoagulation for men with a CHA₂DS₂-VASc score of 1. Take the bleeding risk into account. [new 2014]

Offer anticoagulation to people with a CHA₂DS₂-VASc score of 2 or above, taking bleeding risk into account. [new 2014]

Discuss the options for anticoagulation with the person and base the choice on their clinical features and preferences. [new 2014]

Apixaban

Apixaban is recommended as an option for preventing stroke and systemic embolism within its marketing authorisation, that is, in people with nonvalvular AF with 1 or more risk factors such as:

- Prior stroke or transient ischaemic attack
- Age 75 years or older
- Hypertension
- Diabetes mellitus
- Symptomatic heart failure. [This recommendation is from the NGC summary of the NICE guideline [Apixaban for preventing stroke and systemic embolism in people with nonvalvular atrial fibrillation](#) (NICE technology appraisal guidance 275).] [2013]

The decision about whether to start treatment with apixaban should be made after an informed discussion between the clinician and the person about the risks and benefits of apixaban compared with warfarin, dabigatran etexilate and rivaroxaban. For people who are taking warfarin, the potential risks and benefits of switching to apixaban should be considered in light of their level of INR control. [This recommendation is from the

NGC summary of the NICE guideline [Apixaban for preventing stroke and systemic embolism in people with nonvalvular atrial fibrillation](#) (NICE technology appraisal guidance 275).] [2013]

Dabigatran Etxilate

Dabigatran etexilate is recommended as an option for the prevention of stroke and systemic embolism within its licensed indication, that is, in people with nonvalvular AF with one or more of the following risk factors:

- Previous stroke, transient ischaemic attack or systemic embolism
- Left ventricular ejection fraction below 40%
- Symptomatic heart failure of New York Heart Association (NYHA) class 2 or above
- Age 75 years or older
- Age 65 years or older with one of the following: diabetes mellitus, coronary artery disease or hypertension. [This recommendation is from the NGC summary of the NICE guideline [Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation](#) (NICE technology appraisal guidance 249).] [2012]

The decision about whether to start treatment with dabigatran etexilate should be made after an informed discussion between the clinician and the person about the risks and benefits of dabigatran etexilate compared with warfarin. For people who are taking warfarin, the potential risks and benefits of switching to dabigatran etexilate should be considered in light of their level of INR control. [This recommendation is from the NGC summary of the NICE guideline [Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation](#) (NICE technology appraisal guidance 249).] [2012]

Rivaroxaban

Rivaroxaban is recommended as an option for the prevention of stroke and systemic embolism within its licensed indication, that is, in people with nonvalvular AF with one or more risk factors such as:

- Congestive heart failure
- Hypertension
- Age 75 years or older
- Diabetes mellitus
- Prior stroke or transient ischaemic attack. [This recommendation is from [Rivaroxaban for the prevention of stroke and systemic embolism in people with atrial fibrillation](#) (NICE technology appraisal guidance 256).] [2012]

The decision about whether to start treatment with rivaroxaban should be made after an informed discussion between the clinician and the person about the risks and benefits of rivaroxaban compared with warfarin. For people who are taking warfarin, the potential risks and benefits of switching to rivaroxaban should be considered in light of their level of INR control. [This recommendation is from [Rivaroxaban for the prevention of stroke and systemic embolism in people with atrial fibrillation](#) (NICE technology appraisal guidance 256).] [2012]

Assessing Anticoagulation Control with Vitamin K Antagonists

Calculate the person's time in therapeutic range (TTR) at each visit. When calculating TTR:

- Use a validated method of measurement such as the Rosendaal method for computer-assisted dosing or proportion of tests in range for manual dosing
- Exclude measurements taken during the first 6 weeks of treatment
- Calculate TTR over a maintenance period of at least 6 months. [new 2014]

Reassess anticoagulation for a person with poor anticoagulation control shown by any of the following:

- 2 INR values higher than 5 or 1 INR value higher than 8 within the past 6 months
- 2 INR values less than 1.5 within the past 6 months
- TTR less than 65%. [new 2014]

When reassessing anticoagulation, take into account and if possible address the following factors that may contribute to poor anticoagulation control:

- Cognitive function
- Adherence to prescribed therapy

- Illness
- Interacting drug therapy
- Lifestyle factors including diet and alcohol consumption. [new 2014]

If poor anticoagulation control cannot be improved, evaluate the risks and benefits of alternative stroke prevention strategies and discuss these with the person. [new 2014]

Self-monitoring and Self-management of Vitamin K Antagonists

NICE is developing diagnostics guidance on Self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have AF or heart valve disease: point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) (publication expected August 2014).

Antiplatelets

Do not offer aspirin monotherapy solely for stroke prevention to people with AF. [new 2014]

Review of People with AF

For people who are not taking an anticoagulant, review stroke risk when they reach age 65 or if they develop any of the following at any age:

- Diabetes
- Heart failure
- Peripheral arterial disease
- Coronary heart disease
- Stroke, transient ischaemic attack or systemic thromboembolism [new 2014]

For people who are not taking an anticoagulant because of bleeding risk or other factors, review stroke and bleeding risks annually, and ensure that all reviews and decisions are documented. [new 2014]

For people who are taking an anticoagulant, review the need for anticoagulation and the quality of anticoagulation at least annually, or more frequently if clinically relevant events occur affecting anticoagulation or bleeding risk. [new 2014]

Left Atrial Appendage Occlusion

Consider left atrial appendage occlusion (LAAO) if anticoagulation is contraindicated or not tolerated and discuss the benefits and risks of LAAO with the person. For more information see [Percutaneous occlusion of the left atrial appendage in non-valvular atrial fibrillation for the prevention of thromboembolism](#) [] (NICE interventional procedure guidance 349). [new 2014]

Do not offer LAAO as an alternative to anticoagulation unless anticoagulation is contraindicated or not tolerated. [new 2014]

Rate and Rhythm Control

When to Offer Rate or Rhythm Control

Offer rate control as the first-line strategy to people with AF, except in people:

- Whose AF has a reversible cause
- Who have heart failure thought to be primarily caused by AF
- With new-onset AF
- With atrial flutter whose condition is considered suitable for an ablation strategy to restore sinus rhythm
- For whom a rhythm control strategy would be more suitable based on clinical judgement. [new 2014]

Rate Control

Offer either a standard beta-blocker (that is, a beta-blocker other than sotalol) or a rate-limiting calcium-channel blocker as initial monotherapy to people with AF who need drug treatment as part of a rate control strategy. Base the choice of drug on the person's symptoms, heart rate, comorbidities and preferences when considering drug treatment. [new 2014]

Consider digoxin monotherapy for people with non-paroxysmal AF only if they are sedentary (do no or very little physical exercise). [new 2014]

If monotherapy does not control symptoms, and if continuing symptoms are thought to be due to poor ventricular rate control, consider

combination therapy with any 2 of the following:

- A beta-blocker
- Diltiazem
- Digoxin [new 2014]

Do not offer amiodarone for long-term rate control. [new 2014]

Rhythm Control

Consider pharmacological and/or electrical rhythm control for people with AF whose symptoms continue after heart rate has been controlled or for whom a rate-control strategy has not been successful. [new 2014]

Cardioversion

For people having cardioversion for AF that has persisted for longer than 48 hours, offer electrical (rather than pharmacological) cardioversion. [new 2014]

Consider amiodarone therapy starting 4 weeks before and continuing for up to 12 months after electrical cardioversion to maintain sinus rhythm, and discuss the benefits and risks of amiodarone with the person. [new 2014]

For people with AF of greater than 48 hours' duration, in whom elective cardioversion is indicated:

- Both TOE-guided cardioversion and conventional cardioversion should be considered equally effective
- A TOE-guided cardioversion strategy should be considered:
 - Where experienced staff and appropriate facilities are available and
 - Where a minimal period of precardioversion anticoagulation is indicated due to the person's choice or bleeding risks. [2006]

Drug Treatment for Long-term Rhythm Control

Assess the need for drug treatment for long-term rhythm control, taking into account the person's preferences, associated comorbidities, risks of treatment and likelihood of recurrence of AF. [new 2014]

If drug treatment for long-term rhythm control is needed, consider a standard beta-blocker (that is, a beta-blocker other than sotalol) as first-line treatment unless there are contraindications. [new 2014]

If beta-blockers are contraindicated or unsuccessful, assess the suitability of alternative drugs for rhythm control, taking comorbidities into account. [new 2014]

Dronedarone is recommended as an option for the maintenance of sinus rhythm after successful cardioversion in people with paroxysmal or persistent AF:

- Whose AF is not controlled by first-line therapy (usually including beta-blockers), that is, as a second-line treatment option and after alternative options have been considered and
- Who have at least 1 of the following cardiovascular risk factors:
 - Hypertension requiring drugs of at least 2 different classes
 - Diabetes mellitus
 - Previous transient ischaemic attack, stroke or systemic embolism
 - Left atrial diameter of 50 mm or greater or
 - Age 70 years or older and
- Who do not have left ventricular systolic dysfunction and
- Who do not have a history of, or current, heart failure. [This recommendation is from the NICE guideline Dronedarone for the treatment of non-permanent atrial fibrillation (NICE technology appraisal guidance 197).] [2010, amended 2012]

People who do not meet the criteria in the recommendation above who are currently receiving dronedarone should have the option to continue treatment until they and their clinicians consider it appropriate to stop. [This recommendation is from the NICE guideline Dronedarone for the treatment of non-permanent atrial fibrillation (NICE technology appraisal guidance 197).] [2010, amended 2012]

Consider amiodarone for people with left ventricular impairment or heart failure. [new 2014]

Do not offer class 1c antiarrhythmic drugs such as flecainide or propafenone to people with known ischaemic or structural heart disease. [new

2014]

Where people have infrequent paroxysms and few symptoms, or where symptoms are induced by known precipitants (such as alcohol, caffeine), a 'no drug treatment' strategy or a 'pill-in-the-pocket' strategy should be considered and discussed with the person. [2006] A 'pill-in-the-pocket' strategy is defined as the person managing paroxysmal atrial fibrillation themselves by taking antiarrhythmic drugs only when an episode of atrial fibrillation starts.

In people with paroxysmal AF, a 'pill-in-the-pocket' strategy should be considered for those who:

- Have no history of left ventricular dysfunction, or valvular or ischaemic heart disease and
- Have a history of infrequent symptomatic episodes of paroxysmal AF and
- Have a systolic blood pressure greater than 100 mmHg and a resting heart rate above 70 beats per minute (bpm) and
- Are able to understand how to, and when to, take the medication. [2006]

Left Atrial Ablation and a Pace and Ablate Strategy

Left Atrial Ablation

If drug treatment has failed to control symptoms of AF or is unsuitable:

- Offer left atrial catheter ablation to people with paroxysmal AF
- Consider left atrial catheter or surgical ablation for people with persistent AF
- Discuss the risks and benefits with the person.* [new 2014]

Consider left atrial surgical ablation at the same time as other cardiothoracic surgery for people with symptomatic AF.† [new 2014]

*For more information on left atrial catheter ablation see [Percutaneous balloon cryoablation for pulmonary vein isolation in atrial fibrillation](#) [] (NICE interventional procedure guidance 427), [Percutaneous endoscopic catheter laser balloon pulmonary vein isolation for atrial fibrillation](#) [] (NICE interventional procedure guidance 399) and [Percutaneous \(non-thoroscopic\) epicardial catheter radiofrequency ablation for atrial fibrillation](#) [] (NICE interventional procedure guidance 294). For more information on left atrial surgical ablation without thoracotomy see [Thoracoscopic epicardial radiofrequency ablation for atrial fibrillation](#) [] (NICE interventional procedure guidance 286).

†For more information on left atrial surgical ablation at the same time as other cardiothoracic surgery see [High-intensity focused ultrasound for atrial fibrillation in association with other cardiac surgery](#) [] (NICE interventional procedure guidance 184), [Cryoablation for atrial fibrillation in association with other cardiac surgery](#) [] (NICE interventional procedure guidance 123), [Microwave ablation for atrial fibrillation in association with other cardiac surgery](#) [] (NICE interventional procedure guidance 122) and [Radiofrequency ablation for atrial fibrillation in association with other cardiac surgery](#) [] (NICE interventional procedure guidance 121).

Pace and Ablate Strategy

Consider pacing and atrioventricular node ablation for people with permanent AF with symptoms or left ventricular dysfunction thought to be caused by high ventricular rates. [new 2014]

When considering pacing and atrioventricular node ablation, reassess symptoms and the consequent need for ablation after pacing has been carried out and drug treatment further optimised. [new 2014]

Consider left atrial catheter ablation before pacing and atrioventricular node ablation for people with paroxysmal AF or heart failure caused by non-permanent (paroxysmal or persistent) AF. [new 2014]

Management for People Presenting Acutely with AF

Rate and Rhythm Control

Carry out emergency electrical cardioversion, without delaying to achieve anticoagulation, in people with life-threatening haemodynamic instability caused by new-onset AF. [new 2014]

In people with AF presenting acutely with haemodynamic instability, offer rate or rhythm control if the onset of the arrhythmia is less than 48 hours, and start rate control if it is more than 48 hours or is uncertain. [new 2014]

Consider either pharmacological or electrical cardioversion depending on clinical circumstances and resources in people with new-onset atrial fibrillation who will be treated with a rhythm control strategy. [new 2014]

If pharmacological cardioversion has been agreed on clinical and resource grounds for new-onset atrial fibrillation, offer:

- Flecainide or amiodarone if there is no evidence of structural or ischaemic heart disease or
- Amiodarone if there is evidence of structural heart disease. [new 2014]

In people with AF in whom the duration of the arrhythmia is greater than 48 hours or uncertain and considered for long-term rhythm control, delay cardioversion until they have been maintained on therapeutic anticoagulation for a minimum of 3 weeks. During this period offer rate control as appropriate. [2006, amended 2014]

Do not offer magnesium or a calcium-channel blocker for pharmacological cardioversion. [new 2014]

Anticoagulation

In people with new-onset AF who are receiving no, or subtherapeutic, anticoagulation therapy:

- In the absence of contraindications, offer heparin at initial presentation
- Continue heparin until a full assessment has been made and appropriate antithrombotic therapy has been started, based on risk stratification (see recommendations under "Assessment of Stroke and Bleeding Risks" and "Interventions to Prevent Stroke"). [2006, amended 2014]

In people with a confirmed diagnosis of AF of recent onset (less than 48 hours since onset), offer oral anticoagulation if:

- Stable sinus rhythm is not successfully restored within the same 48-hour period following onset of AF or
- There are factors indicating a high risk of AF recurrence‡ or
- It is recommended under "Assessment of Stroke and Bleeding Risks" and "Interventions to Prevent Stroke". [2006, amended 2014]

In people with new-onset AF where there is uncertainty over the precise time since onset, offer oral anticoagulation as for persistent AF (see "Assessment of Stroke and Bleeding Risks" and "Interventions to Prevent Stroke"). [2006, amended 2014]

‡Factors indicating a high risk of atrial fibrillation recurrence include: a history of failed attempts at cardioversion; structural heart disease (mitral valve disease, left ventricular dysfunction or an enlarged left atrium); a prolonged history of atrial fibrillation (more than 12 months); previous recurrences of atrial fibrillation.

Initial Management of Stroke and AF

For guidance on the initial management of stroke and AF see recommendations in the NICE guideline [Stroke. Diagnosis and initial management of acute stroke and transient ischaemic attack \(TIA\)](#) [redacted] (NICE clinical guideline 68). [new 2014]

Prevention and Management of Postoperative AF

In people undergoing cardiothoracic surgery:

- Reduce the risk of postoperative AF by offering 1 of the following:
 - Amiodarone
 - A standard beta-blocker (that is, a beta-blocker other than sotalol)
 - A rate-limiting calcium antagonist
- Do not offer digoxin. [2006, amended 2014]

In people undergoing cardiothoracic surgery on pre-existing beta-blocker therapy, continue this treatment unless contraindications develop (such as postoperative bradycardia or hypotension). [2006, amended 2014]

Unless contraindicated, offer a rhythm-control strategy as the initial management option for the treatment of postoperative AF following cardiothoracic surgery. [2006, amended 2014]

Unless contraindicated, manage postoperative atrial fibrillation following non-cardiothoracic surgery as for new-onset AF with any other precipitant. [2006, amended 2014]

In the prophylaxis and management of postoperative AF, use appropriate antithrombotic therapy and correct identifiable precipitants (such as electrolyte imbalance or hypoxia). [2006, amended 2014]

Definitions:

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some

interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GDG usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally 'must' (or 'must not') is used if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. Similar forms of words (for example, 'Do not offer...') are used when the GDG is confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GDG uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Clinical Algorithm(s)

The following clinical algorithms are provided in the full version of the original guideline document (see the "Availability of Companion Documents" field):

- Stroke prevention of people with nonvalvular AF
- Rate control strategies
- Rhythm control strategies
- Left atrial ablation strategies

A NICE pathway titled "Atrial Fibrillation Overview" is available from the [National Institute for Health and Care Excellence \(NICE\) Web site](#)

Scope

Disease/Condition(s)

Atrial fibrillation

Guideline Category

Diagnosis

Evaluation

Management

Prevention

Risk Assessment

Treatment

Clinical Specialty

Cardiology

Emergency Medicine

Family Practice

Geriatrics

Internal Medicine

Pulmonary Medicine

Intended Users

Advanced Practice Nurses

Health Care Providers

Hospitals

Nurses

Patients

Physician Assistants

Physicians

Public Health Departments

Guideline Objective(s)

- To offer best practice advice on the care of adults (aged 18 and over) with suspected or diagnosed atrial fibrillation (AF)
- To address several clinical areas in which new evidence has become available, including stroke and bleeding risk stratification, the role of new antithrombotic agents and ablation strategies

Target Population

Adults (18 years or older) with atrial fibrillation (AF), including paroxysmal (recurrent), persistent and permanent AF, and atrial flutter

Note: This guideline does not apply to people with congenital heart disease precipitating AF.

Interventions and Practices Considered

Diagnosis/Evaluation

1. Manual pulse palpation
2. Electrocardiogram (ECG; ambulatory, standard)
3. Echocardiography (transoesophageal, transthoracic)
4. Assessment of stroke and bleeding risks using validated tools (HAS-BLED, CHA₂DS₂-VASc)

Treatment/Management/Prevention

1. Personalised package of care and information
2. Referral for specialised management
3. Anticoagulation
 - Apixaban
 - Dabigatran etexilate

- Rivaroxaban
- Assessment of coagulation control with vitamin K antagonists
- Antiplatelets (aspirin, not recommended as monotherapy for stroke prevention)
- Heparin
- Left atrial appendage occlusion (LAAO)

4. Rate and rhythm control

- Beta blockers
- Calcium channel blockers
- Diltiazem
- Digoxin
- Combination therapy
- Electrical cardioversion followed by amiodarone or dronedarone
- Left atrial ablation

Major Outcomes Considered

- Cardioversion success rate
- Recurrence of atrial fibrillation (AF) following successful cardioversion
- Restoration and maintenance of sinus rhythm
- Incidence of stroke or thromboembolism
- Mortality (all-cause and vascular)
- Efficacy of antiarrhythmic drugs
- Side effects of drugs
- Health-related quality of life
- Hospitalisations and rehospitalisations for AF
- Development of heart failure

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Developing the Review Questions and Outcomes

Review questions were developed in a PICO framework (patient, intervention, comparison and outcome) for intervention reviews, and with a framework of population, presence or absence of factors under investigation (for example prognostic factors) and outcomes for prognostic reviews.

This use of a framework guided the literature searching process, critical appraisal and synthesis of evidence, and facilitated the development of recommendations by the Guideline Development Group (GDG). The review questions were drafted by the NCGC technical team and refined and validated by the GDG. The questions were based on the key clinical areas identified in the scope (see Appendix A in the full version of the original guideline document [see the "Availability of Companion Documents" field]).

A total of 18 review questions were identified.

Full literature searches, critical appraisals and evidence reviews were completed for all the specified review questions.

Searching for Evidence

Clinical Literature Search

Systematic literature searches were undertaken to systematically identify all published clinical evidence relevant to the review questions. Searches were undertaken according to the parameters stipulated within the Guidelines Manual 2012 (see the "Availability of Companion Documents" field). Databases were searched using relevant medical subject headings, free-text terms and study-type filters where appropriate. Studies published in languages other than English were not reviewed. Where possible, searches were restricted to articles published in English. All searches were conducted in MEDLINE, EMBASE, and The Cochrane Library. Additional subject specific databases were used for some questions: Cumulative Index to Nursing and Allied Health Literature (CINAHL) for referral and education; Health Management Information Consortium (HMIC) for referral; PsycINFO for education. Databases were searched from their date of inception, and all searches were updated on 3 October 2013. No papers published after this date were considered.

Search strategies were quality assured by cross-checking reference lists of highly relevant papers, analysing search strategies in other systematic reviews, and asking GDG members to highlight any additional studies. The questions, the study types applied, the databases searched and the years covered can be found in Appendix F in the full version of the original guideline document.

The titles and abstracts of records retrieved by the searches were sifted for relevance, with potentially significant publications obtained in full text. These were assessed against the inclusion criteria.

During the scoping stage, a search was conducted for guidelines and reports on the websites listed below and on organisations relevant to the topic. Searching for grey literature or unpublished literature was not undertaken. All references sent by stakeholders were considered.

- Guidelines International Network database (www.g-i-n.net)
- National Guideline Clearinghouse (www.guideline.gov/)
- National Institute for Health and Care Excellence (NICE) (www.nice.org.uk)
- National Institutes of Health Consensus Development Program (consensus.nih.gov/)
- National Library for Health (www.library.nhs.uk/)

Health Economic Literature Search

Systematic literature searches were also undertaken to identify health economic evidence within published literature relevant to the review questions. The evidence was identified by conducting a broad search relating to atrial fibrillation in the National Health Service Economic Evaluation Database (NHS EED), the Health Technology Assessment (HTA) database and the Health Economic Evaluations Database (HEED) with no date restrictions. Additionally, the search was run on MEDLINE and EMBASE using a specific economic filter, from 2010, to ensure recent publications that had not yet been indexed by the economic databases were identified. Studies published in languages other than English were not reviewed. Where possible, searches were restricted to articles published in English.

The health economic search strategies are included in Appendix F in the full version of the original guideline document. All searches were updated on 3 October 2013. No papers published after this date was considered.

Evidence of Effectiveness

The evidence was reviewed following the steps shown schematically in Figure 1 in the full version of the original guideline document:

- Potentially relevant studies were identified for each review question from the search results by reviewing titles and abstracts. Full papers were then obtained.
- Full papers were reviewed against pre-specified inclusion and exclusion criteria to identify studies that addressed the review question in the appropriate population (review protocols are included in Appendix C in the full version of the original guideline document).

Inclusion and Exclusion Criteria

The inclusion and exclusion of studies was based on the review protocols, which can be found in Appendix C in the full version of the original guideline document. Excluded studies by review question (with the reasons for their exclusion) are listed in Appendix J in the full version of the original guideline document. The GDG was consulted about any uncertainty regarding inclusion or exclusion.

Randomised trials, non-randomised trials, and observational studies (including prognostic studies) were included in the evidence reviews as appropriate.

Literature reviews, posters, letters, editorials, comment articles, unpublished studies and studies not in English were excluded.

The review protocols are presented in Appendix C in the full version of the original guideline document.

Type of Studies

For most intervention reviews in this guideline, parallel randomised controlled trials (RCTs) were included because they are considered the most robust type of study design that could produce an unbiased estimate of the intervention effects. If the GDG believed RCT data were not appropriate or there was limited evidence from RCTs, well-conducted non-randomised studies were included. Please refer to Appendix C in the full version of the original guideline document for full details on the study design of studies selected for each review question. For example the monitoring and referral to specialist care reviews included non-randomised controlled trials if there were no RCTs available. It was considered unlikely that the search would find any RCTs.

For prognostic reviews, prospective and retrospective cohort studies were included. Case-control studies were not included. Studies of lower risk of bias were preferred, taking into account the analysis and the study design for example studies with more than 100 events. Studies which applied and assessed the different tools within the cohort were preferred to compare the tools predictive and discriminatory power Data were not combined in meta-analyses for prognostic studies.

Where data from observational studies were included, the GDG decided that the results for each outcome should be presented separately for each study and meta-analysis was not conducted.

Evidence of Cost-effectiveness

The GDG is required to make decisions based on the best available evidence of both clinical and cost effectiveness. Guideline recommendations should be based on the expected costs of the different options in relation to their expected health benefits (that is, their "cost-effectiveness") rather than the total implementation cost. Thus, if the evidence suggests that a strategy provides significant health benefits at an acceptable cost per patient treated, it should be recommended even if it would be expensive to implement across the whole population.

Evidence on cost-effectiveness related to the key clinical issues being addressed in the guideline was sought. The health economist:

- Undertook a systematic review of the published economic literature.
- Undertook new cost-effectiveness analysis in priority areas.

Literature Review

The health economist:

- Identified potentially relevant studies for each review question from the economic search results by reviewing titles and abstracts. Full papers were then obtained.
- Reviewed full papers against pre-specified inclusion and exclusion criteria to identify relevant studies (see below for details).
- Critically appraised relevant studies using the economic evaluations checklist as specified in the Guidelines Manual.
- Extracted key information about the studies' methods and results into evidence tables (included in Appendix H in the full version of the original guideline document).
- Generated summaries of the evidence in NICE economic evidence profiles (included in the relevant chapter for each review question) – see below for details.

Inclusion and Exclusion Criteria

Full economic evaluations (studies comparing costs and health consequences of alternative courses of action: cost-utility, cost-effectiveness, cost-benefit and cost-consequence analyses) and comparative costing studies that addressed the review question in the relevant population were considered potentially includable as economic evidence.

Studies that only reported cost per hospital (not per patient), or only reported average cost effectiveness without disaggregated costs and effects, were excluded. Literature reviews, abstracts, posters, letters, editorials, comment articles, unpublished studies and studies not in English were excluded.

Remaining studies were prioritised for inclusion based on their relative applicability to the development of this guideline and the study limitations.

For example, if a high quality, directly applicable United Kingdom (UK) analysis was available, then other less relevant studies may not have been included. Where selective exclusions occurred on this basis, this is noted in the relevant section.

For more details about the assessment of applicability and methodological quality see the economic evaluation checklist (see Appendix E of the Guidelines Manual and the health economics review protocol in Appendix C in the full version of the original guideline document).

When no relevant economic studies were found from the economic literature review, relevant UK NHS unit costs related to the compared interventions were presented to the GDG to inform the possible economic implications of the recommendations.

Number of Source Documents

The number of studies identified for each aspect of clinical and health economics literature is provided in Appendices G and H in the full version of the original guideline document, respectively (see the "Availability of Companion Documents" field).

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Overall Quality of Outcome Evidence in Grading of Recommendations Assessment, Development and Evaluation (GRADE)

Level	Description
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Evidence of Effectiveness

The evidence was reviewed following the steps shown schematically in Figure 1 in the full version of the original guideline document (see the "Availability of Companion Documents" field):

- Relevant studies were critically appraised using the appropriate checklist as specified in the Guidelines Manual.
- Key information was extracted on the study's methods, PICO (patient, intervention, comparison and outcome) factors and results. These were presented in summary tables (in each review chapter) and evidence tables (see Appendix G in the full version of the original guideline document).

- Summaries of evidence were generated by outcome (included in the relevant review chapters) and were presented in Guideline Development Group (GDG) meetings:
 - Randomised studies: data were meta-analysed where appropriate and reported in Grading of Recommendations Assessment, Development, Development and Evaluation (GRADE) profiles (for intervention reviews).
 - Prognostic studies: data were presented as medians and range of scores.

Methods of Combining Clinical Studies

Data Synthesis for Intervention Reviews

Where possible, meta-analyses were conducted to combine the results of studies for each review question using Cochrane Review Manager (RevMan5) software. Fixed-effects (Mantel-Haenszel) techniques were used to calculate risk ratios (relative risk) for the binary outcomes: mortality, stroke or thromboembolic complications, rehospitalisation, ischaemic stroke, haemorrhagic stroke, major bleeding, procedural complications, restoration of sinus rhythm recurrence of atrial fibrillation (AF), rate of discontinuation due to adverse events, number of patients referred to anticoagulation clinics.

For continuous outcomes, measures of central tendency (mean) and variation (standard deviation) were required for meta-analysis. Data for continuous outcomes (quality of life, time in therapeutic international normalised ratio [INR] range, anxiety, and decision conflict and knowledge scores) were analysed using an inverse variance method for pooling weighted mean differences and, where the studies had different scales, standardised mean differences were used. A generic inverse variance option in RevMan5 was used if any studies reported solely the summary statistics and 95% confidence interval (CI) or standard error (SE); this included any hazard ratios (HRs) reported. However, in cases where standard deviations were not reported per intervention group, the SE for the mean difference was calculated from other reported statistics (p values or 95% CIs); meta-analysis was then undertaken for the mean difference and SE using the generic inverse variance method in RevMan5. When the only evidence was based on studies that summarised results by presenting medians (and interquartile ranges), or only p values were given, this information was assessed in terms of the study's sample size and was included in the GRADE tables without calculating the relative or absolute effects. Consequently, aspects of quality assessment such as imprecision of effect could not be assessed for evidence of this type.

Where reported, time-to-event data was presented as a hazard ratio.

For a number of reviews, the results were presented separately for pre-stratified groups or strata. Strata included:

- Heart failure
- Reversible causes of AF
- Acute unstable AF

For more details on these strata refer to the protocols (see Appendix C in the full version of the original guideline document).

Statistical heterogeneity was assessed by visually examining the forest plots, and by considering the chi-squared test for significance at $p < 0.1$ or an I-squared inconsistency statistic (with an I-squared value of more than 50% indicating considerable heterogeneity).

The means and standard deviations of continuous outcomes were required for meta-analysis. However, in cases where standard deviations were not reported, the standard error was calculated if the p values or 95% CIs were reported and meta-analysis was undertaken with the mean and standard error (SE) using the generic inverse variance method in RevMan5. Where p values were reported as 'less than', a conservative approach was undertaken. For example, if p value was reported as ' $p < 0.001$ ', the calculations for standard deviations will be based on a p value of 0.001. If these statistical measures were not available then the methods described in Section 16.1.3 of the Cochrane Handbook (September 2009) 'Missing standard deviations' were applied as the last resort.

For interpretation of the binary outcome results, differences in the absolute event rate were calculated using the GRADEpro software, for the median event rate across the control arms of the individual studies in the meta-analysis. Absolute risk differences were presented in the GRADE profiles and in clinical summary of findings tables, for discussion with the GDG.

For binary outcomes, absolute event rates were also calculated using the GRADEpro software using event rate in the control arm of the pooled results.

Network Meta-analysis (NMA)

A NMA was conducted for the review on choice of antithrombotic therapy for stroke prevention. This type of analysis simultaneously compares multiple treatments in a single meta-analysis, preserving the randomisation of randomized controlled trials (RCTs) included in the reviews of direct comparisons trials. The aim of the NMA was to include all relevant evidence in order both to answer questions on the clinical effectiveness of

interventions when no direct comparison was available and to give a ranking of treatments in terms of efficacy. The output was expressed as the probability of each antithrombotic treatment being the best for an outcome and as effect estimates for how much each treatment is better than the other treatments included in the network.

A random effects Bayesian NMA was performed using the software WinBUGS version 1.4. That allowed inclusion of multi-arm trials and accounts for the correlation between arms in the trials with any number of trial arms.

There were 3 main outputs from the NMA:

- Estimated HRs (with their 95% credible intervals) were calculated for comparisons of the direct and indirect evidence.
- The probability that each treatment was best, based on the proportion of Markov chain iterations in which each treatment had the highest probability of achieving the outcomes selected in the network(s).
- A ranking of treatments compared to baseline groups (presented as the median rank and its 95% credible intervals).

A full technical account can be found in Appendix M in the full version of the original guideline document.

Data Synthesis for Prognostic Factor and Risk Tool Reviews

Odds ratios (ORs), risk ratios (RRs) or HRs, with their 95% CIs for the effect of the pre-specified prognostic factors combined within a risk stratification tool were extracted from the papers. In addition, sensitivity and specificity for each risk stratification tool were considered if reported.

The area under the receiver operated characteristic (ROC) curve (AUC) data for each study was reported as the c-statistic. The AUC describes the overall prognostic accuracy in regards to the tests discriminatory power across the full range of thresholds. The GDG agreed on the following criteria for AUC:

- ≤ 0.50 : worse than chance
- 0.50–0.60: very poor
- 0.61–0.70: poor
- 0.71–0.80: moderate
- 0.81–0.92: good
- 0.91–1.00: excellent or perfect test

Heterogeneity or inconsistency amongst studies was visually inspected in the forest plots where appropriate (only when there were similar thresholds).

Appraising the Quality of Evidence by Outcomes

The evidence for outcomes from the included RCTs and, where appropriate, observational studies were evaluated and presented using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group (<http://www.gradeworkinggroup.org/>). The software developed by the GRADE working group (GRADEpro) was used to assess the quality of each outcome, taking into account individual study quality factors and the meta-analysis results. Results were presented in GRADE profiles ('GRADE tables'), which consist of 2 sections: the 'Clinical evidence profile' table includes details of the quality assessment while the 'Clinical evidence summary of findings' table includes pooled outcome data, where appropriate, an absolute measure of intervention effect and the summary of quality of evidence for that outcome. In this table, the columns for intervention and control indicate summary measures and measures of dispersion (such as mean and standard deviation or median and range) for continuous outcomes and frequency of events (n/N: the sum across studies of the number of patients with events divided by sum of the number of completers) for binary outcomes. Reporting or publication bias was taken into consideration in the quality assessment and only included in the 'Clinical evidence profile' table if it was apparent from GDG members.

The evidence for each outcome was examined separately for the quality elements listed and defined in Table 2 in the full version of the original guideline document. Each element was graded using the quality levels listed in Table 3 in the full version of the original guideline document. The main criteria considered in the rating of these elements are discussed below. Footnotes were used to describe reasons for grading a quality element as having serious or very serious problems. The ratings for each component were summed to obtain an overall assessment for each outcome (see Table 4 in the full version of the original guideline document).

The GRADE toolbox is currently designed only for randomised trials and observational studies but we adapted the quality assessment elements and outcome presentation for prognostic studies.

Grading the Quality of Clinical Evidence

After results were pooled, the overall quality of evidence for each outcome was considered. The following procedure was adopted when using GRADE:

1. A quality rating was assigned, based on the study design. RCTs start as High, observational studies as Low, and uncontrolled case series as Low or Very low.
2. The rating was then downgraded for the specified criteria: risk of bias (study limitations), inconsistency, indirectness, imprecision and publication bias. These criteria are detailed in the full version of the guideline. Evidence from observational studies (which had not previously been downgraded) was upgraded if there was: a large magnitude of effect, a dose–response gradient, and if all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results showed no effect. Each quality element considered to have 'serious' or 'very serious' risk of bias was rated down by 1 or 2 points respectively.
3. The downgraded or upgraded marks were then summed and the overall quality rating was revised. For example, all RCTs started as High and the overall quality became Moderate, Low or Very low if 1, 2 or 3 points were deducted, respectively.
4. The reasons or criteria used for downgrading were specified in the footnotes.

The details of the criteria used for each of the main quality elements are discussed further in Sections 3.4.6 to 3.4.9 in the full version of the original guideline document.

Evidence of Cost-effectiveness

The GDG is required to make decisions based on the best available evidence of both clinical and cost effectiveness. Guideline recommendations should be based on the expected costs of the different options in relation to their expected health benefits (that is, their 'cost effectiveness') rather than the total implementation cost. Thus, if the evidence suggests that a strategy provides significant health benefits at an acceptable cost per patient treated, it should be recommended even if it would be expensive to implement across the whole population.

Evidence on cost-effectiveness related to the key clinical issues being addressed in the guideline was sought. The health economist:

- Undertook a systematic review of the published economic literature.
- Undertook new cost-effectiveness analysis in priority areas.

Literature Review

The health economist:

- Critically appraised relevant studies using the economic evaluations checklist as specified in The Guidelines Manual.
- Extracted key information about the studies' methods and results into evidence tables (included in Appendix H in the full version of the original guideline document).
- Generated summaries of the evidence in NICE economic evidence profiles (included in the relevant chapter for each review question).

NICE Economic Evidence Profiles

The NICE economic evidence profile has been used to summarise cost and cost-effectiveness estimates. The economic evidence profile shows an assessment of applicability and methodological quality for each economic evaluation, with footnotes indicating the reasons for the assessment. These assessments were made by the health economist using the economic evaluation checklist from The guidelines manual. It also shows the incremental costs, incremental effects (for example, quality-adjusted life years [QALYs]) and incremental cost-effectiveness ratio for the base case analysis in the evaluation, as well as information about the assessment of uncertainty in the analysis. See Table 6 in the full version of the original guideline document for more details.

If a non-UK study was included in the profile, the results were converted into pounds sterling using the appropriate purchasing power parity.

Methods Used to Formulate the Recommendations

Expert Consensus

Informal Consensus

Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on

behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

The Guideline Development Group (GDG)

A multidisciplinary Guideline Development Group (GDG) comprising health professionals and researchers as well as lay members developed this guideline. The GDG was convened by the NCGC and chaired by Dr. Campbell Cowan in accordance with guidance from NICE. The group met every 6 weeks during the development of the guideline. Staff from the NCGC provided methodological support and guidance for the development process. The team working on the guideline included a project manager, systematic reviewers, health economists and information scientists. They undertook systematic searches of the literature, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate and drafted the guideline in collaboration with the GDG.

Developing Recommendations

Over the course of the guideline development process, the GDG was presented with:

- Evidence tables of the clinical and economic evidence reviewed from the literature. All evidence tables are in Appendices G and H of the full version of the original guideline document.
- Summary of clinical and economic evidence and quality (as presented in Chapters 6–19 in the full version of the original guideline document).
- Forest plots and summary receiver operating characteristic (ROC) curves (see Appendix I in the full version of the original guideline document).
- A description of the methods and results of the cost-effectiveness analysis(es) undertaken for the guideline (see Appendix L in the full version of the original guideline document).

Recommendations were drafted on the basis of the GDG interpretation of the available evidence, taking into account the balance of benefits, harms and costs between different courses of action. This was either done formally in an economic model, or informally. Firstly, the net benefit over harm (clinical effectiveness) was considered, focusing on the critical outcomes. When this was done informally, the GDG took into account the clinical benefits and harms when one intervention was compared with another. The assessment of net benefit was moderated by the importance placed on the outcomes (the GDG's values and preferences), and the confidence the GDG had in the evidence (evidence quality). Secondly, it was assessed whether the net benefit justified any differences in costs.

When clinical and economic evidence was of poor quality, conflicting or absent, the GDG drafted recommendations based on their expert opinion. The considerations for making consensus-based recommendations include the balance between potential harms and benefits, the economic costs compared to the economic benefits, current practices, and recommendations made in other relevant guidelines, patient preferences and equality issues. The consensus recommendations were agreed through discussions in the GDG. The GDG considered whether the uncertainty was sufficient to justify delaying making a recommendation to await further research, taking into account the potential harm of failing to make a clear recommendation (see Appendix P in the full version of the original guideline document).

The wording of recommendations was agreed by the GDG and focused on the following factors:

- The actions health professionals need to take.
- The information readers need to know.
- The strength of the recommendation (for example the word "offer" was used for strong recommendations and "consider" for weak recommendations).
- The involvement of patients (and their carers if needed) in decisions on treatment and care.
- Consistency with NICE's standard advice on recommendations about drugs, waiting times and ineffective interventions.

The main considerations specific to each recommendation are outlined in the "Recommendations and link to evidence" sections within each chapter.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some

interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GDG usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally 'must' (or 'must not') is used if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. Similar forms of words (for example, 'Do not offer...') are used when the GDG is confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GDG uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Cost Analysis

Undertaking New Health Economic Analysis

As well as reviewing the published economic literature for each review question, as described above, new economic analysis was undertaken by the health economist in selected areas. Priority areas for new health economic analysis were agreed by the Guideline Development Group (GDG) after formation of the review questions and consideration of the available health economic evidence.

The GDG identified the prevention of stroke and decision rules to identify and select low risk patients who would benefit from anticoagulation as the highest priority area for original economic modelling. This was due to having sufficient data to parameterise the model in a clinical topic area where the health and cost implications are large. A detailed pathway model developed by Brunel University was made available for the purposes of the guideline. It was felt that this model should be simplified and focus in particular on stroke prevention to avoid the potential for poorer quality data and assumptions regarding other clinical topics in the pathway to impact on the conclusions the analysis.

The following general principles were adhered to in developing the cost-effectiveness analysis:

- Methods were consistent with the National Institute for Health and Care Excellence (NICE) reference case.
- The GDG was involved in the design of the model, selection of inputs and interpretation of the results.
- Model inputs were based on the systematic review of the clinical literature supplemented with other published data sources where possible.
- When published data was not available GDG expert opinion was used to populate the model.
- Model inputs and assumptions were reported fully and transparently.
- The results were subject to sensitivity analysis and limitations were discussed.
- The model was peer-reviewed by another health economist at the National Clinical Guideline Centre (NCGC).

Cost-effectiveness Criteria

NICE's report 'Social value judgements: principles for the development of NICE guidance' sets out the principles that GDGs should consider when judging whether an intervention offers good value for money. In general, an intervention was considered to be cost effective if either of the following criteria applied (given that the estimate was considered plausible):

- The intervention dominated other relevant strategies (that is, it was both less costly in terms of resource use and more clinically effective compared with all the other relevant alternative strategies), or
- The intervention cost less than £20,000 per quality-adjusted life-year (QALY) gained compared with the next best strategy.

If the GDG recommended an intervention that was estimated to cost more than £20,000 per QALY gained, or did not recommend one that was estimated to cost less than £20,000 per QALY gained, the reasons for this decision are discussed explicitly in the 'Recommendations and link to evidence' section of the relevant chapter, with reference to issues regarding the plausibility of the estimate or to the factors set out in 'Social value judgements: principles for the development of NICE guidance'.

In the Absence of Economic Evidence

When no relevant published studies were found, and a new analysis was not prioritised, the GDG made a qualitative judgement about cost effectiveness by considering expected differences in resource use between options and relevant UK National Health Service (NHS) unit costs, alongside the results of the clinical review of effectiveness evidence. The UK NHS costs reported in the guideline were those presented to the GDG and they were correct at the time recommendations were drafted; they may have been revised subsequently by the time of publication. However, we have no reason to believe they have been changed substantially.

See Appendix L, Cost-effectiveness of stroke prevention strategies in patients with atrial fibrillation (AF), in the full version of the guideline document.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

This guidance is subject to a 6-week public consultation and feedback as part of the quality assurance and peer review of the document. All comments received from registered stakeholders are responded to in turn and posted on the National Institute for Health and Care Excellence (NICE) website.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of individuals with atrial fibrillation (AF)

See the "Trade off between clinical benefits and harms" sections in the full version of the original guideline document (see the "Availability of Companion Documents" field) for additional details about benefits of specific interventions.

Potential Harms

- The decision to commence a drug for stroke prevention involves consideration of a balance between the benefits in stroke reduction, the adverse effects of increased bleeding risk and particularly the increased risk of haemorrhagic stroke. The use of risk stratification tools to assess both stroke risk and bleeding risk are considered in Chapters 8 and 10 in the full version of the original guideline document (see the "Availability of Companion Documents" field).
- The Guideline Development Group (GDG) expressed caution about the use of verapamil and diltiazem in patients with heart failure. Apart from this, there was thought to be no evidence to manage patients with heart failure differently from atrial fibrillation (AF) patients as a whole.
- Amiodarone has monitoring requirements to reduce the likelihood of adverse side effects and events. For example, dronedarone which is initiated in hospital with specialist input, requires regular monitoring of liver function tests (before treatment, 1 week and 1 month after initiation of treatment, then monthly for 6 months, then every 3 months for 6 months and periodically thereafter) and electrocardiogram

(ECG) every 6 months. Amiodarone can cause serious adverse reactions affecting the eyes, heart, lung, liver, thyroid gland, skin and peripheral nervous system. Because these reactions may be delayed, patients on long-term treatment require on-going supervision.

- Drugs used for the maintenance of sinus rhythm have side effects. Moreover, the restoration of sinus rhythm may lead to a false sense of security regarding stroke risk and to the discontinuation of anticoagulant therapy. The risk of stroke is still present should AF recur, and often happens asymptotically.
- There is an increased risk of bradycardia associated with the use of beta-blockers and nausea associated with procainamide, as well as with amiodarone when loaded rapidly in the pre-operative period.
- Procedural complications such as cardioversion-related thromboembolism
- The short term risks for left atrial appendage occlusion (LAAO) included cardiac tamponade, thromboembolism and device embolisation.

See the "Trade off between clinical benefits and harms" sections in the full version of the original guideline document (see the "Availability of Companion Documents" field) for additional details about benefits of specific interventions.

Contraindications

Contraindications

- In people undergoing cardiothoracic surgery on pre-existing beta-blocker therapy, continue this treatment unless contraindications develop (such as postoperative bradycardia or hypotension).
- A prosthetic mechanical heart valve is a contraindication for clopidogrel or for oral anticoagulant
- The authors considered antiplatelet therapy to have limited benefits for atrial fibrillation (AF) patients in preventing strokes and made a strong recommendation that aspirin should not be offered to patients at increased risk of stroke.
- The presence of heart failure specifically contraindicated the use of the class I anti-arrhythmics propafenone and flecainide, and of the class III agent dronedarone.

Qualifying Statements

Qualifying Statements

- This guidance represents the view of National Institute for Health and Care Excellence (NICE), which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summaries of product characteristics of any drugs.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.
- Treatment and care should take into account individual needs and preferences. Patients should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If the patient is under 16, their family or carers should also be given information and support to help the child or young person to make decisions about their treatment. Healthcare professionals should follow the [Department of Health's advice on consent](#) [redacted]. If someone does not have capacity to make decisions, healthcare professionals should follow the [code of practice that accompanies the Mental Capacity Act](#) [redacted] and the [supplementary code of practice on deprivation of liberty safeguards](#) [redacted].
- NICE has produced guidance on the components of good patient experience in adult National Health Service (NHS) services. All healthcare professionals should follow the recommendations in [Patient experience in adult NHS services](#) [redacted].
- The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.
- For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision.

Implementation of the Guideline

Description of Implementation Strategy

Implementation tools and resources to help you put the guideline into practice are also available from the [National Institute for Health and Care Excellence \(NICE\) Web site](#) .

Key Priorities for Implementation

The following recommendations have been identified as priorities for implementation.

Personalised Package of Care and Information

Offer people with atrial fibrillation a personalised package of care. Ensure that the package of care is documented and delivered, and that it covers:

- Stroke awareness and measures to prevent stroke
- Rate control
- Assessment of symptoms for rhythm control
- Who to contact for advice if needed
- Psychological support if needed
- Up-to-date and comprehensive education and information on:
 - Cause, effects and possible complications of atrial fibrillation
 - Management of rate and rhythm control
 - Anticoagulation
 - Practical advice on anticoagulation in line with recommendations in NICE clinical guideline 144
 - Support networks (for example, cardiovascular charities). [new 2014]

Referral for Specialised Management

Refer people promptly at any stage if treatment fails to control the symptoms of atrial fibrillation and more specialised management is needed. [new 2014] (The Guideline Development Group defined 'promptly' as no longer than 4 weeks after the final failed treatment or no longer than 4 weeks after recurrence of atrial fibrillation following cardioversion when further specialised management is needed.)

Assessment of Stroke and Bleeding Risks

Stroke Risk

Use the CHA₂DS₂-VASc stroke risk score to assess stroke risk in people with any of the following:

- Symptomatic or asymptomatic paroxysmal, persistent or permanent atrial fibrillation
- Atrial flutter
- A continuing risk of arrhythmia recurrence after cardioversion back to sinus rhythm. [new 2014]

Bleeding Risk

Use the HAS-BLED score to assess the risk of bleeding in people who are starting or have started anticoagulation. Offer modification and monitoring of the following risk factors:

- Uncontrolled hypertension
- Poor control of international normalised ratio (INR) ("labile INRs")
- Concurrent medication, for example concomitant use of aspirin or a non-steroidal anti-inflammatory drug (NSAID)
- Harmful alcohol consumption. [new 2014]

Interventions to Prevent Stroke

Anticoagulation

Anticoagulation may be with apixaban, dabigatran etexilate, rivaroxaban or a vitamin K antagonist.

- Offer anticoagulation to people with a CHA₂DS₂-VASc score of 2 or above, taking bleeding risk into account. [new 2014]

Assessing Anticoagulation Control with Vitamin K Antagonists

Calculate the person's time in therapeutic range (TTR) at each visit. When calculating TTR:

- Use a validated method of measurement such as the Rosendaal method for computer-assisted dosing or proportion of tests in range for manual dosing
- Exclude measurements taken during the first 6 weeks of treatment
- Calculate TTR over a maintenance period of at least 6 months. [new 2014]

If poor anticoagulation control cannot be improved, evaluate the risks and benefits of alternative stroke prevention strategies and discuss these with the person. [new 2014]

Antiplatelets

Do not offer aspirin monotherapy solely for stroke prevention to people with atrial fibrillation. [new 2014]

Rate and Rhythm Control

When to Offer Rate or Rhythm Control

Offer rate control as the first-line strategy to people with atrial fibrillation, except in people:

- Whose atrial fibrillation has a reversible cause
- Who have heart failure thought to be primarily caused by atrial fibrillation
- With new-onset atrial fibrillation
- With atrial flutter whose condition is considered suitable for an ablation strategy to restore sinus rhythm
- For whom a rhythm control strategy would be more suitable based on clinical judgement. [new 2014]

Left Atrial Ablation and a Pace and Ablate Strategy

Left Atrial Ablation

If drug treatment has failed to control symptoms of atrial fibrillation or is unsuitable:

- Offer left atrial catheter ablation to people with paroxysmal atrial fibrillation
- Consider left atrial catheter or surgical ablation for people with persistent atrial fibrillation
- Discuss the risks and benefits with the person.* [new 2014]

*For more information on left atrial catheter ablation see [Percutaneous balloon cryoablation for pulmonary vein isolation in atrial fibrillation](#) [] (NICE interventional procedure guidance 427), [Percutaneous endoscopic catheter laser balloon pulmonary vein isolation for atrial fibrillation](#) [] (NICE interventional procedure guidance 399) and [Percutaneous \(non-thoracoscopic\) epicardial catheter radiofrequency ablation for atrial fibrillation](#) [] (NICE interventional procedure guidance 294). For more information on left atrial surgical ablation without thoracotomy see [Thoracoscopic epicardial radiofrequency ablation for atrial fibrillation](#) [] (NICE interventional procedure guidance 286).

Implementation Tools

Clinical Algorithm

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents and Patient Resources* fields below.

Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Clinical Guideline Centre. Atrial fibrillation: the management of atrial fibrillation. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Jun. 49 p. (Clinical guideline; no. 180).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

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Guideline Committee

Guideline Development Group

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Financial Disclosures/Conflicts of Interest

At the start of the guideline development process all Guideline Development Group (GDG) members declared interests including consultancies, fee-paid work, share-holdings, fellowships and support from the healthcare industry. At all subsequent GDG meetings, members declared arising conflicts of interest.

Members were either required to withdraw completely or for part of the discussion if their declared interest made it appropriate. The details of declared interests and the actions taken are shown in Appendix B in the full version of the original guideline document (see the "Availability of Companion Documents" field).

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Collaborating Centre for Chronic Conditions. Atrial fibrillation. National clinical guideline for management in primary and secondary care. London (UK): Royal College of Physicians; 2006. 173 p. [380 references].

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Electronic copies: Available from the [National Institute for Health and Care Excellence \(NICE\) Web site](#) .

Availability of Companion Documents

The following are available:

- Atrial fibrillation: the management of atrial fibrillation. Full guideline. London (UK): National Institute for Health and Care Excellence; 2014 Jun. 420 p. (Clinical guideline; no. 180). Electronic copies: Available in from the [National Institute for Health and Care Excellence \(NICE\) Web site](#) .
- Atrial fibrillation: the management of atrial fibrillation. Appendices A-R. London (UK): National Institute for Health and Care Excellence; 2014 Jun. 656 p. (Clinical guideline; no. 180). Electronic copies: Available from the [NICE Web site](#) .
- Atrial fibrillation: the management of atrial fibrillation. Appendix S. London (UK): National Institute for Health and Care Excellence; 2014 Jun. 172 p. (Clinical guideline; no. 180). Electronic copies: Available from the [NICE Web site](#) .
- Atrial fibrillation: the management of atrial fibrillation. Baseline assessment tool. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Jun. (Clinical guideline; no 180). Electronic copies: Available from the [NICE Web site](#) .
- Atrial fibrillation: the management of atrial fibrillation. Costing report. London (UK): National Institute for Health and Care Excellence; 2014 Jun. 25 p. (Clinical guideline; no. 180). Electronic copies: Available from the [NICE Web site](#) .
- Atrial fibrillation: the management of atrial fibrillation. Costing template. London (UK): National Institute for Health and Care Excellence; 2014 Jun. (Clinical guideline; no. 180). Electronic copies: Available from the [NICE Web site](#) .
- Patient decision aid: user guide for healthcare professionals. Implementing the NICE guideline on atrial fibrillation (CG180). London (UK): National Institute for Health and Care Excellence; 2014 Jun. 11 p. (Clinical guideline; no. 180). Electronic copies: Available from the [NICE Web site](#) .
- Guidelines manual 2012. London (UK): National Institute for Health and Care Excellence; 2012 Nov. Electronic copies: Available from the [NICE Archive Web site](#) .

Patient Resources

The following are available:

- Atrial fibrillation. Information for the public. London (UK): National Institute for Care Excellence (NICE); 2014 Jun. Available from the [National Institute for Health and Care Excellence \(NICE\) Web site](#) . Also available for download as a Kindle or EPUB ebook from the [NICE Web site](#) .
- Atrial fibrillation: medicines to help reduce your risk of a stroke – what are the options? Patient decision aid. London (UK): National Institute for Care Excellence (NICE); 2014 Jun. 36 p. Available from the [NICE Web site](#) .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

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